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EXAMINER

SAIDHA, TEKCHAND

ART UNIT	PAPER NUMBER
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1652

19

DATE MAILED: 01/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/018730

Applicant(s)

Wong, LL

Examiner

T. Saidha

Group Art Unit

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—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 5/20/03
- ☒ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 20, 22-24, 26-28 & 35 is/are pending in the application.
- Of the above claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 20, 22-24, 26-28 & 35 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____.
 - ☐ received in this national stage application from the International Bureau (PCT Rule 1.7.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s) 18
- ☐ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other _____

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FINAL REJECTION

1. Applicant's arguments filed as per the amendment dated May 19, 2003 have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).
2. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.
3. Claims 20, 22-24, 26-28 and 35 are under consideration in this examination.
4. Non-elected claims 29-34 & 36-37, following restriction, remain pending and which claims have been previously withdrawn from consideration. These claims will have to be canceled upon identification of allowable subject matter.
5. ***Claim Rejections - 35 U.S.C. § 112 (first paragraph)***

Written Description

Claims 20, 22-24, 26-28 and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 20, 22-24, 26-28 and 35 are drawn to a process for oxidizing any 'chlorinated aromatic substrate' with more than one chlorine atom, and oxidizing the substrate using any P450cam or P450 monooxygenase from any source (claim 20, 22-24, 26-28 and 35); or where the enzyme is mutated by one or more amino acid(s) of the amino acid; or where amino acid 96 in one

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is substituted for another (claim 24); or where the aromatic compound is benzene or biphenyl (claim 26); or specific substrate, example, 1, 2-dichlorobenzene (claim 27); and where the monooxygenase can be used to decontaminate a locus contaminated with any chlorinated aromatic substrate that has more than one chlorine atom by contacting with the enzyme.

The specification, however, only provides a single representative species of a process of oxidizing halo aromatic substrate, such as 1, 2-dichlorobenzene, ...hexachlorobenzene (see claim 27) using the P450cam from *Pseudomonas putida* of SEQ ID NO : 2 and the mutants based thereof. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species to other species where such sequences are conserved in order to establish a relationship among species or modify the enzyme by substitution of one or amino acid(s) in the active site or make mutant P450cam or monooxygenases by modifying any P450cam or monooxygenase from any source. No description of what positional P-450cam mutants, for example position 87, 96, 98, 101, 185, 244, 247, 248, 296, 395 or 396 of SEQ ID NO : 2, would be equivalent to in another P450cam or monooxygenases sequence(s) is evident. Therefore without reference to a specific SEQ ID NO :, the reference to specific mutational modification remains undescribed. The general knowledge in the art concerning sequence alignments [see Applicants' cited Gotoh (1992) JBC 267(1) : 83-90, especially see page 86, Figure 3, new IDS] dose not provide equivalent or identical amino acid at the claimed mutational position at least with respect to *P. Putida* and mammalian cytochrome P450, in order that a person skilled in the art can determine or extend the guidance provided in modifying SEQ ID NO : 2 (*P. Putida*) to any P450cam or

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monooxygenase and from any source, be it animal, plant or microbial. Further it remains undescribed how the contaminated 'locus' [or surface] can be treated by contacting an enzyme. No such decontaminating formulations are described. The specification also fails to describe additional representative species of these monooxygenases or substrates other than those presented in claim 27, for example, by any identifying structural characteristics such as the properties or activity recited in claims, for which no predictability of structure is apparent. Given this lack of additional representative species, such as those discussed above, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicants' Arguments :

Applicants' key point regarding the rejection, that one skilled in the art could use the alignment of sequences from Gotoh (1992) to determine equivalent functional regions or amino acids of another P450 enzyme(s).

However, contrary to Applicant's claim, Gotoh does not identify any equivalent amino acid positions in his sequence alignments of Figure 3. In discussing the review of literature, Gotoh points that the 'results of these studies have been controversial, and no unified view about substrate recognition sites in mammalian P450s has been established [see page 83, column 2, lines 24-26]. No equivalent functional regions or amino acids positions of another P450 enzyme(s) have been determined. Further, it is pointed out regarding the confusion and difficulty in aligning distantly related protein sequences of mammalian P450 and bacterial P450 101A (P450cam) of *Pseudomonas*

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Putida [see Gotoh (1992), page 83, column 2 paragraph 2] having only 12-20% identity. It would be impossible for one skilled in the art to identify the equivalent amino acid positions from any P450 enzyme(s) (any source) given the teachings of the sequence of SEQ ID NO : 2 which may be modified in the specific positions and be used in the manner claimed.

6. ***Claim Rejections - 35 U.S.C. § 112*** (second paragraph)

Claims 20, 22-24, 26-28 and 35 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 20 & 24 recite specific amino acid position, for example, 87, 96, 98, etc., without a reference sequence. Therefore without reference to a specific SEQ ID NO :, reference to specific mutational modification remains 'indefinite'.

Claims 22-23, 26-28 & 35 are included in the rejection for failing to correct the defect present in the base claim(s).

7. ***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application

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by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claims 20, 22-24, 26-28 and 35 are rejected under 35 U.S.C. 102(b) or 102(e) as being anticipated by WO 96/14419 [Flitsch et al.] or US Patent 6,100,074 [Flitsch et al., same as WO 96/14419] respectively. Flitsch et al. [WO 96/14419, 102(b)] teach a number of specific mutants of mono-oxygenase P-450cam, including position 96 (Y96F mutant) of *Pseudomonas putida* wherein the ring carbon of the substrate is oxidized. Other mutational positions where one or more amino acids are modified in the active site include 87, 98, 101, 185, 193, 244, 147, 295, 297, 395 & 396 (see pages 2, 4 & 11) or by replacing 96Y by a less polar side chain (pages 3 & 4). The reference further teaches the gene and the encoding monooxygenase. The reference also teaches a method of oxidizing halo aromatic compounds, for example, diphenyl and biphenyl compounds and their halogenated variants (see page 4, lines 10-27 and claims 5 & 9). Assay mixture also contained electron transfer reductase; and an **electron transfer redoxin**. Flitsch et al. Also teach how to modify the active site of the wild type monooxygenase in order to decrease its specificity towards camphor, creating a desired 'aromatic pocket' (see pages 3 and 4) which would encourage binding of aromatic side chain (see page 2, 2nd paragraph).

Flitsch et al. also teach oxidation of specific halo aromatic compounds, or one having more than one chlorine molecule [see page 8 (iv), lines 11-13, abstract, Table 4(a)].

The reference [WO 96/14419 (Flitsch et al.) or US Patent 6,100,074 (Flitsch et al.)] teaches all the claim limitations and therefore anticipates the claims.

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8.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20, 22-24, 26-28 and 35 are rejected under the judicially created doctrine of double patenting over claim 8 of U. S. Patent No. 6,100,074 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Claim 8 of USP 6,100,074 is drawn to a method of oxidizing a compound which in the broadest sense will read upon 'chlorinated aromatic compound', using a mono-oxygenase cytochrome P-450cam system, under oxidizing conditions. Claims 20, 22-24, 26-28 and 35 of the instant application are anticipated by the cited patent.

Applicants' Arguments :

Applicants argue that claim 20 now require 'electron transfer redoxin' and this is not present in claim 8 of the USP 6,100,074, the examiner withdraw the double patenting rejection.

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In response Applicants' attention is drawn to paragraph 7 of this Office Action (102 rejection) which explains in detail where the limitation 'electron transfer redoxin' is taught. Further, 'electron transfer redoxin' which mediates the transfer of electron from cofactor is a naturally occurring 'electron transfer redoxin' or protein (see instant specification, page 8, lines 23-28), thus is not only described or taught in the cited patent but does not distinguish between the patented and the currently claimed invention. The rejection is therefore maintained.

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

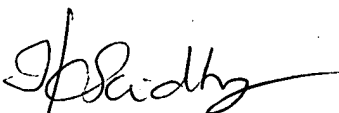
A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (703) 305-6595. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group in the Technology Center is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Tekchand Saidha
Primary Examiner, Art Unit 1652
December 30, 2003